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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PITRAK, JENNIFER S	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
12/01/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/589,823	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	JENNIFER PITRAK	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-31* is/are pending in the application.

4a) Of the above claim(s) *18,22-25 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17, 19-21, 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/15/2007; 09/03/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group IV, claims 17, 19-21, and 26-30 drawn to a method of treatment or prophylaxis comprising using an antisense RNA or an siRNA to modulate TWEAK in the reply filed on 08/28/2008 is acknowledged. Applicant's election without traverse of stroke from the species in claims 26-29 is acknowledged.

Claims 17-31 are pending. Claims 18, 22-25, and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 08/28/2008.

Claims 17, 19-21, and 26-30 are under examination.

Specification

The disclosure is objected to because of the following informalities:

Applicant's attention is directed to the attached Notice to Comply with 37 C.F.R. 1.821 - 1.825. A Computer Readable File (CRF) of the sequence listing is required, but has not been filed in this case. See 37 CFR § 1.821(e). Also, sequences in the specification at pages 14, 16, and 17 are not properly referenced by their SEQ ID NO. See 37 CFR § 1.821(d). Appropriate correction is required.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See, bottom of page 19. Applicant is required to delete the

embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is required.

The use of the trademarks has been noted in this application at least at pages 19-20, including for example, Hyperfilm-ECL, ELISA, and Caspase Glo. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Appropriate correction is required.

Claim Objections

Claim 30 is objected to because of the following informalities: the claim refers to the "medicament" of claim 17. Although there is implicit antecedent basis for this limitation because claim 17 is to a method of treatment, the limitation lacks explicit antecedent basis. The claim would more appropriately refer to "the substance" of claim 17, rather than to "the medicament".

Claim Rejections - 35 USC § 112 and 101

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 17, 19-21, and 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 provides for the use of a substance that modulates or inhibits the expression of TWEAK, but, since the claim does not set forth any steps involved in the method or process, it is unclear what method or process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 17, 19-21, and 26-30 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

For the purpose of claim examination in the interest of compact prosecution, "using a substance" in claim 17 will be interpreted to mean "by administering a substance."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17, 19-21, and 26-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 17 is directed to a method of treating or preventing neurological or psychiatric conditions using a substance that modulates or inhibits the expression or activity of TWEAK. Claims 19-21 specify that the substance is an antisense or an siRNA molecule. Claims 26-30 specify that the neurological condition is at least one condition selected from a neurological disease with pathophysiological mechanisms involving ischemia or hypoxia, a neurological disease with pathophysiological mechanisms involving ischemia and hypoxia, a neurodegenerative disease, and a disease of the nervous system accompanied by neural cell death, including stroke.

According to the instant specification, the term “substance” is to be understood broadly and means all of the material means which directly or indirectly bring about the desired effect (p.6, lines 24-30). The specification provides a list of examples of such substances, to which the term is not limited. This list of possible examples includes nucleic acids, protein, natural or artificial binding partners of TWEAK or the TWEAK receptor, antibodies, antagonists of the TWEAK receptor, peptidomimetics of a TWEAK receptor antagonist, antisense nucleic acids, aptamers, natural or artificial transcription factors, nucleic acid constructs, vectors, and low molecular weight compounds (p.6, lines 24-30). Also according to the instant specification, "modulate" means increase or decrease of at least one essential property or of the expression of TWEAK (p.6, lines 32-36). "Treatment" is broadly defined as slowing, interrupting, arresting, or stopping the progression of the disease or condition and "prophylaxis" means any degree of

inhibition of the time of onset or severity of signs or symptoms of the disease or condition, including, but not limited to, the complete prevention of the disease or condition (p.7, lines 4-9). The neurological and psychiatric conditions disclosed in the specification include ischemic stroke, hemorrhagic stroke, amyotrophic lateral sclerosis (ALS), Parkinson's Disease, cerebral ischemia, traumatic brain injury, cardiovascular disease, multiple sclerosis, schizophrenia, and others (pages 2-6; page 12, line 20 to page 13, line 2). These diseases are described as having several disease manifestations or symptoms, each of which may or may not be associated with TWEAK activity or expression. Thus, the individual claim terms are extremely broad, reading on methods of treating a nearly unlimited number of disease symptoms with nearly unlimited substances that either increase or decrease the expression or activity of TWEAK.

The precise structure of the substances that provide the claimed function of modulating TWEAK are not described by the instant specification nor by the art such that one of skill in the art would recognize possession of such substances. Insofar as the claims are directed to the elected invention, antisense oligonucleotides or siRNAs that directly inhibit TWEAK expression by targeting the TWEAK coding sequence, though not described in the instant specification, are readily identifiable by those of skill in the art. However, the elected invention encompasses methods comprising antisense oligonucleotides and siRNAs that target genes other than TWEAK that are involved in TWEAK expression or activity, such as genes involved in upregulating or inhibiting TWEAK expression or TWEAK receptor intracellular signaling. Therefore, even within the elected invention, the genus of TWEAK modulators is very broad and is not adequately described in the instant specification or in the art by complete or partial structure, such as nucleotide sequence or target gene. Furthermore, the claims in their broader scope

encompass methods of using other TWEAK modulators such as proteins, natural or artificial binding partners of TWEAK or the TWEAK receptor, antagonists of the TWEAK receptor, peptidomimetics of a TWEAK receptor antagonist, natural or artificial transcription factors, nucleic acid constructs, vectors, and low molecular weight compounds, which are not readily identifiable. The many TWEAK antagonists and agonists encompassed by the claims may also act indirectly on TWEAK.

In summary, the substances disclosed as useful in the instantly claimed methods are not adequately described to demonstrate that Applicant had possession of the invention at the time of filing. The structure of the TWEAK modulators encompassed by the claims is not described by sufficient complete or partial structure or by a representative number of species either by the instant specification or by the art such that one of skill would recognize that Applicant had possession of the invention at the time of filing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 19, 21, and 26-30 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wiley (2002, U.S. PGPub 2002/0041876).

The claims are to a method for the treatment and prophylaxis of a neurological or psychiatric conditions, specifically stroke, by administering a substance that modulates the

activity or expression of TWEAK (claims 17, and 26-29), wherein the substance is an antisense oligonucleotide and is provided by a viral vector (claims 19 and 21), and wherein the administered substance further comprises additional factors (claim 30).

Wiley teaches methods of treating and preventing angiogenic-dependent diseases, such as ischemia of the brain (stroke) by administering an antisense nucleic acid targeted to TWEAK (page 8, paragraph 101; page 9 paragraphs 106 and 107). At page 9, paragraph 110, Wiley teaches that the antisense nucleic acids are typically administered with additional factors, such as pharmaceutically acceptable carriers. At page 10, paragraph 119, Wiley teaches that the nucleic acid sequences can be delivered with viral delivery systems such as retroviral and adenoviral vectors. Thus, Wiley anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17, 19-21, and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiley as applied to claims 17, 19, 21, and 26-30 above, and further in view of Bass (2001, Nature, v.411:428-9) and Elbashir, et al. (2001, Nature, v.411:494-8).

The claims are to a method for the treatment and prophylaxis of neurological or psychiatric conditions, specifically stroke, by administering a substance that modulates the activity or expression of TWEAK (claims 17, and 26-29), wherein the substance is an antisense

or an siRNA oligonucleotide and is provided by a viral vector (claims 19-21), and wherein the administered substance further comprises additional factors (claim 30).

Wiley teaches the administration of antisense oligonucleotides for decreasing TWEAK expression and treating stroke as described in the preceding rejection. Wiley does not teach the use of siRNAs for decreasing TWEAK expression.

Bass teaches that RNA interference, mediated by double-stranded small interfering RNAs (siRNAs), has proven to be more robust than antisense techniques in that it works more often and typically decreases expression of a gene to lower levels than do antisense oligonucleotides or eliminates expression entirely (p.429. top of first column). Bass further states that in mammalian cells, siRNAs are effective at concentrations that are several orders of magnitude below the concentrations typically used in antisense experiments (p.429 top of first column). Elbashir, et al. teach that siRNAs are 21- and 22-nucleotide RNA duplexes that supress gene expression in mammalian cells (abstract).

It would have been obvious to one of skill in the art at the time of the instant invention to administer antisense oligonucleotides to inhibit TWEAK expression as taught by Wiley. It further would have been obvious to use siRNAs to inhibit TWEAK expression in place of antisense oligonucleotides because Bass teaches that siRNAs are more effective than antisense oligonucleotides at inhibiting target gene expression and Elbashir, et al. teach the structure of siRNAs. Thus, the claims would have been obvious at the time of the instant invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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